The Microbiome and Irritable Bowel Syndrome

An Emerging Hope for Treatment

ABSTRACT
Irritable bowel syndrome (IBS) is a gastrointestinal disorder that affects 15%–20% of the US population. Its symptoms can have negative effects on a person’s quality of life, and its treatment can be associated with high medical costs. An emerging area of irritable bowel syndrome research concerns the relationship between this condition and the gut microbiome. The purpose of this article is not only to review irritable bowel syndrome, and the role that the microbiome can play in its symptoms, but also to examine new emerging pathways that could blaze the trail for more individualized treatments. If equipped with this knowledge, gastrointestinal nurses and providers of care can be better prepared to help patients with irritable bowel syndrome in order to manage symptoms and improve their quality of life.

Background
IBS is a GI disorder marked by abdominal pain and a change in bowel habits. No single test exists to diagnose it. The Rome IV criteria are, however, widely used to assist in the diagnosis of IBS (Lacy & Patel, 2017). These criteria describe specific symptoms over a period of time. For a patient to be officially diagnosed with IBS using the Rome IV criteria, he or she must report symptoms of abdominal pain, coupled with a change in bowel habits, one or more days a week for at least 3 months. Symptoms of abdominal pain should be associated with pain during defecation (relieved or worsened by bowel movement) or change in stool form or frequency. Alarm features identified through a thorough history and physical examination that warrant further testing to rule out other illnesses include, but are not limited to, anemia, unintentional weight loss, hematochezia, and a family history of colon cancer.

IBS classification of the various subtypes is based on the most frequent bowel symptom. Subtypes are defined on the basis of whether constipation, diarrhea, mixed (both diarrhea and constipation), and undefined subtype are predominant (Lacy & Patel, 2017). Specific bowel habits can be further characterized using the Bristol stool form scale (BSFS) (Lewis & Heaton, 1997). The BSFS is helpful to review with patients because the detailed description it provides on stool consistency enhances the quality of patient symptom diaries and self-reflection. The BSFS recognizes seven key stool types (Lewis & Heaton, 1997):
The provider may find it helpful for patients to describe the consistency of stools in a symptom diary to help tailor treatment more efficiently. Managing IBS, however, requires a multifaceted approach such as examining diet, the role of serotonin (5-HT), microbiome pathways, and stress that would impact management of this complex illness.

Impact
Quality of Life
Symptoms of IBS vary but can affect one’s quality of life significantly due to effects on activities of daily living, emotions, and social life (Ballou & Keefer, 2017). For example, abdominal pain can be so severe that an individual will not be able to engage in his or her regular daily activities. Bowel movements can be unpredictable at times and interfere with social activities, necessitating planning events around the bathroom or avoiding them altogether, thus creating isolation. These lifestyle changes cause emotional distress, anxiety, and affect feelings of well-being. Severe and unpredictable symptoms can lead to missed appointments and work commitments, which, in turn, can affect professional relationships and productivity.

Financial
In addition to absenteeism from work due to symptoms, IBS carries financial burden associated with medical visits, testing, and medication costs (Levy et al., 2001). Health providers such as gastroenterology providers, dietitians, or other specialists assist with the diagnosis and management of IBS. Diagnostic testing including colonoscopy, radiographic studies, and laboratory studies are often performed to rule out other diseases/conditions before reaching a diagnosis of IBS. Medications including prescription, over-the-counter, and dietary supplements are often recommended. At times, symptoms become severe, necessitating an emergency department or urgent care visit. Overall, IBS carries a substantial economic load on the healthcare system, with direct medical expenses ranging from $1.5 billion to 10 billion a year (Saljoughian, 2023).

Role of Serotonin
Serotonin is a neurotransmitter that plays a role in influencing intestinal motility and sensitivity, as well as brain–gut communication (Mittal et al., 2017). The gut microbiome is involved in the production of serotonin; therefore, imbalances affect levels of this neurotransmitter that can lead to gut dysfunction and symptoms. Examining these relationships can shed some light on how serotonin affects IBS patients.

Motility
Serotonin not only regulates emotions and mood but also is a neurotransmitter that regulates muscle contractions in the intestines or peristalsis (Mittal et al., 2017). Serotonin regulates peristalsis by influencing the sensitivity and motility of the gut. In individuals with IBS, alterations in serotonin signaling lead to abnormal gut motility patterns, such as increased or decreased contractions, which contribute to common IBS symptoms such as diarrhea or constipation.

Sensitivity
Serotonin also modulates the sensitivity of the gut to pain, including the patient’s perception of that pain (Appleton, 2018). An imbalance in serotonin receptor activity leads to increased sensitivity to pain in the gut. This heightened sensitivity results in increased abdominal pain and discomfort, which are common complaints of IBS.

Brain–Gut Communication and Medications
Altered serotonin signaling in IBS can influence the gut–brain axis, the communication pathway between the brain and the gut (Appleton, 2018). It also plays a role in the emotional factors that influence IBS symptoms, such as stress.

Serotonin is a signaling molecule that plays a role in peristalsis, so alterations with this signaling contribute to symptoms of IBS. Many medications affect serotonin receptors or levels that help manage symptoms of IBS (Lembo et al., 2022). Tegaserod is a 5-HT4 receptor agonist that enhances activity of serotonin in the gut, promoting peristalsis and chloride secretion to help relieve constipation. Selective serotonin reuptake inhibitors (SSRIs) such as citalopram, sertraline, and fluoxetine change visceral hypersensitivity and gut motility and have been shown to help some symptoms of IBS. SSRIs play a role in IBS but have not been defined sufficiently (Creed, 2006). 5-HT3 antagonists block the action of serotonin to decrease the frequency of stool for patients with diarrhea-predominant IBS (IBS-D). Some providers may tend to prescribe off-label options such as tricyclic antidepressants that are not Federal Drug Administration (FDA) approved (Peyton
Further research is needed to understand the role of serotonin in IBS more fully and to develop more targeted and effective treatments (Appleton, 2018).

Treatments

Various treatments of IBS such as medications, low fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAP) diet, probiotics, high fiber diet, fecal transplant, and eradicating small bowel bacteria overgrowth show some effective symptom relief. However, not all treatments prove successful for everyone, and an individualized approach is recommended.

Low FODMAP Diet

The most effective evidence-based dietary intervention for IBS is the low FODMAP diet (Halmos, Power, Shepherd, Gibson, & Muir, 2014). FODMAPs are foods that contain carbohydrates that are not well absorbed in the intestines and as a result create fluids that can enter the intestinal lumen and cause bloating, gas, and distention (Ong et al., 2010). Water enters the intestinal lumen through a process called osmotic loading that is triggered by short-chain fatty acids, the digestive by-products of FODMAPs, such as fructose. Osmotic load can be considerably uncomfortable for IBS patients as they already have a dysfunctional motor system and visceral sensitivity (Appleton, 2018). Other important FODMAPs include apples, mangoes, and cherries. Following a variable period of avoidance of these foods (typically 2–3 weeks), IBS patients can reintroduce them slowly into their diet, one at a time, to determine which FODMAPs attenuate their IBS symptoms the most.

Although long-term data are lacking, a low FODMAP diet can help patients if they are instructed properly on the three phases (Lacey et al., 2021). Initially, IBS patients would substitute food with low FODMAPs, followed by a gradual food reintroduction to see what specific foods may be exacerbating symptoms. Finally, a more individualized diet plan is outlined that avoids those identified trigger foods. Overall, 4–6 weeks would be needed to complete the process.

A randomized single-blind crossover trial of 30 patients with IBS and 88 healthy (control) individuals reported that symptoms of pain and bloating were alleviated after just 21 days on a low FODMAP diet (Halmos et al., 2014). Sloan et al. (2018) conducted a parallel randomized controlled trial in 37 adults who consumed a low FODMAP diet with a supplement of maltodextrin or oligofructose 7 g twice daily and found that although the prescribed diet reduced total bacterial count and gas production, it has little effect on colonic volume. Changes in the microbiome are also documented as a result of following a low FODMAP diet that can assist in alleviating symptoms (Sloan et al., 2018).

Fiber

Fiber is an important prebiotic that may help IBS patients, but not all forms of fiber are equally beneficial. Ford, Harris, Lacy, Quigley, and Moayyedi (2018) reported that consumption of soluble fiber, such as psyllium, leads to greater IBS symptom relief than consumption of insoluble fiber, such as bran. The impact of bran (insoluble fiber) on IBS symptoms was also reviewed and found it was associated with no significant benefits for the patients involved. Psyllium or ispaghula fiber was looked at in six studies (involving 321 patients) and showed a positive significant effect on symptoms. When discussing diet with an IBS patient, it is therefore important to educate them about benefits and consequences of consuming soluble and insoluble fibers. The American College of Gastroenterology guidelines recommends 25–35 g of fiber a day (Lacey et al., 2021). Overall, fiber has many health benefits and, although not completely understood, assists metabolism, the gut microbiome, and bile acid absorption. Soluble fiber is often recommended in IBS patients, but how much one can tolerate can differ. Increasing dietary fiber should be done at a slower pace to avoid worsening symptoms.

Probiotics

Probiotics (beneficial bacteria) can interfere with harmful bacteria that invade the colonic mucosa and assist with immune activation (Chey, 2019). Probiotics can also affect bile acid metabolism that assists in colonization of beneficial bacteria. Research has shown that the consumption of probiotic supplements can be beneficial for IBS patients. Shortfalls, however, exist if the individualized probiotic supplements taken by patients are not tailored to their specific symptoms (Chey, 2019).

Rifaximin

Rifaximin is often used for patients with small intestinal bacteria overgrowth (SIBO) that is related to IBS. Menees, Maneerattanaporn, Kim, and Chey (2012) conducted a meta-analysis review on the efficacy of the antibiotic rifaximin as a treatment option for IBS. These authors found rifaximin to be more efficacious than a placebo for global IBS symptom alleviation. They also found that older and female patients had higher responses than the other participants. Rifaximin proved to be effective over the placebo in relieving bloating and symptoms of IBS patients.
Small Intestinal Bacterial Overgrowth
The connection between SIBO and IBS is not well-defined and may yet prove to be unrelated (Shaikh, Sun, Canakis, Park, & Weber, 2023). Although an association between SIBO and IBS is generally accepted in many GI practices, characterizing this relationship remains a challenge. A meta-analysis of 48 studies that examined more than 6,500 patients with SIBO found that about half of these patients were diagnosed with SIBO via a breath test. The prevalence of SIBO among patients diagnosed with IBS can range, however, between 4% and 78%. Further high-quality studies are therefore needed to better understand this complex relationship between SIBO and IBS.

Fecal Transplant
Fecal microbiota transplant (FMT) is a procedure that involves the transplantation of a donor’s fecal matter into the recipient to create a healthy microbiome (Johnsen et al., 2018). A study of 90 participants randomly assigned to have FMT or a placebo found that the transplant provided significant symptom relief for patients with IBS. Although the study population was small, it demonstrated that microbiome manipulation via FMT can alleviate IBS symptoms (Johnsen et al., 2018). More recently, El-Salhy, Patcharatrakul, and Gonlachanvit (2021) have also shown that changes in the intestinal bacteria and fermentation patterns, specifically to the short-chain fatty acids, can play a significant role in IBS symptom alleviation in patients who have been treated with FMT. More research is required, however, to examine the role that donor profile, fecal maternal dose, and transplant route plays in the success of FMT.

Food Allergies and Intolerances
The American College of Gastroenterology does not recommend testing for food allergies unless there is a specific food concern (Lacy et al., 2021). Aside from allergies, IBS patients are more likely to identify reactions to food that are not necessarily an allergy. With the low prevalence of food allergies in the adult population, individuals with IBS are less likely to develop food allergies but may exhibit food intolerances (Lacey et al., 2021).

Gas-producing foods such as beans, onions, celery, carrots, bananas, apricots, brussels sprouts, prunes, and wheat germ, simple carbohydrates such as pretzels and bagels, and alcohol and caffeine should be avoided by IBS patients. This is because IBS patients have an underlying visceral hypersensitivity that may explain the extra discomfort they experience when consuming these types of foods (Hasler & Owyang, 2003). Although IBS patients do not have to be lactose intolerant, a lactose-restricted diet may help with bloating issues. Individuals with IBS may be intolerant to milk components such as cow milk protein and fat or have an allergy to dairy. Some may tolerate milk from other mammals or ingestion of soy. Individuals with IBS who have specific food intolerances to these foods would benefit from avoiding them. Taking the time to review these and other possible triggers is essential.

Previous Treatments Versus Current
IBS treatments with medications to target specific symptoms have also been used over the years. Laxatives such as polyethylene glycol 3350 were studied in adolescents with constipation-predominant IBS (IBS-C). Findings showed laxatives helped with constipation but not with abdominal pain (Peyton & Greene, 2014). Further research is also needed to understand the complex role of serotonin in IBS to help target treatment more effectively (Appleton, 2018).

Historically, exclusion diets have been the mainstay for treating IBS from a lifestyle perspective. Although studies reveal that patients identify various food intolerances that can exacerbate their condition and historically exclusion diets were and still are routinely discussed, it is not recommended to perform allergy testing or exclusion diets (Peyton & Greene, 2014). Melchior et al. (2022) highlight that although food restriction and avoidance are known to alleviate IBS symptoms, for some individuals, the symptoms that they experience become so severe that the imposed food restrictions lead to an overall decrease in their quality of life and nutrition deficiencies. This poses the question of how much should be restricted for an individual with IBS? Answering this question remains challenging, but moving away from blanket restrictions and focusing on more specific targets while examining the microbiome and its relationship to the body may be more effective.

Microbiome
The microbiome is composed of various microorganisms (e.g., bacteria, viruses, fungi) that reside in one’s gut and play a significant role in the development and management of IBS (Menees & Chey, 2018). The microbiome ecosystem of a healthy gut usually consists of trillions of various microorganisms that live in the bowels. This ecosystem contributes to one’s health by aiding nutrient absorption, supporting the immune system, and protecting against harmful microorganisms (Rinninella et al., 2019). The gut microbiome also helps maintain the integrity of the intestinal barrier, which acts as a protective layer between the gut and the rest of the body. When the microbiome is disrupted, the intestinal barrier can become compromised, leading to increased intestinal permeability. This process can
allow toxins, bacteria, and other substances to enter the bloodstream, which trigger inflammation and exacerbate IBS symptoms. This phenomenon is called gut dysbiosis.

**Gut Dysbiosis**

Gut dysbiosis is an imbalance in the microbiome characterized by a decrease in beneficial bacteria and an increase in potentially harmful bacteria. Variables that can cause gut dysbiosis include diet, stress, and genetics. If confirmation of gut dysbiosis is desired, a patient’s stool would need to be examined in a laboratory setting, which is not always convenient for many patients with IBS or other chronic illnesses.

Because the microbiome interacts closely with the immune system, an imbalance of the microbiome leads to immune system dysfunction that can cause inflammation and abnormal immune responses (Belkaid & Hand, 2014). These alterations contribute to various illnesses and diseases, including IBS (Zheng, Liwinski, & Elinav, 2020). Current approaches to assist with dysbiosis include modification of diet, supplementation of the diet through the addition of probiotics and prebiotics, and in some cases, fecal transplant. Although it is sensible to review patients’ diet and discuss the use of such interventions with them, our understanding of the benefits of doing so is complex and still evolving.

**Connections**

Imbalances in gut microbial composition and function can contribute to the development and symptoms of conditions such as IBS, inflammatory bowel disease, and constipation (Marchesi et al., 2016; Rajilić-Stojanović et al., 2015). When gut microbiota changes lead to a change in balance of the microbiome ecosystem, changes in the barrier of the intestines, gas production, neurotransmitters, and immune systems occur too. When intestinal lining permeability changes occur, toxins or other bacteria can trigger an immune response and cause inflammation. This leads to differences in fermentation and gas production that can cause abdominal pain/bloating and flatus.

Labus et al. (2017) identified two groups of IBS patients: one with a healthy microbiome, and one with alterations (dysbiosis). The subgroup with dysbiosis had specific brain features; their sensory regions were larger than those with a healthy microbiome. These sensory regions identified in this study receive input from the body about sensations such as pain. Although gut dysbiosis is not necessarily essential to produce IBS symptoms, these findings demonstrate a clear link between the gut, the microbiome, and the brain.

Another important finding in Labus et al.’s study for its dysbiosis group participants is that they experienced significantly more early life stress events (such as death of a parent, a divorce, or abuse) than IBS patients with a healthy microbiome. This study suggests that the distress events that these participants experienced could have sent signals to their brain that changed the environment in which the microbes in their gut developed, which, in turn, could have influenced their brain and gut microbiome development in early life. Although a causal relationship has yet to be established, this suggestion does raise important questions about the relationship between the brain and the gut and the communication between them in IBS patients.

**New Pathways and Targets**

Alterations in the microbiome and microbial metabolites have been linked to GI function and IBS symptom flares in a subset of patients (Mars et al., 2020). Our understanding of the role that it plays in the development of this disease is, however, incomplete due to the lack of human studies (Mars et al., 2020). There has been some movement with specific subtypes and how their symptoms are related to the microbiome. The microbiome’s composition and functions can relate to symptoms of IBS. Some examples including various metabolites such as purine and hypoxanthine as well as bacterial compounds such as tryptamine and their relationship with IBS.

**Purine**

Specific changes in metabolites have been linked to specific symptoms of IBS. For example, purine metabolism can be considered a pathway related to symptoms of IBS. Mars et al. (2020) examined the relationship between diet and symptoms of IBS patients. They found that purine metabolism is the process of breakdown and synthesis of purine compounds. These compounds affect cellular energy. When there are imbalances in the gut, it affects purine metabolism that can influence IBS symptoms.

Certain bacteria such as *Enterobacteriaceae* contribute to excessive purine compounds, leading to more uric acid (a by-product of purine metabolism). Increased uric acid levels are associated with inflammation and hypersensitivity of the gut. When purine metabolism is altered, this affects neurotransmitters in the intestines and leads to symptoms of IBS. Purine metabolites, such as uric acid, also affect the immune system and stimulate inflammation that can lead to pain and changes in the bowels (Mars et al., 2020). Purine starvation therefore, may act as a therapeutic focus for IBS. Unraveling some of the biological relationships in the gut ecosystem may improve our understanding of how these symptoms occur and pave the way for the development of more individualized treatments of IBS.
Metabolites
Another example of how the microbiome is connected to IBS is the metabolite hypoxanthine. Hypoxanthine plays an important role in keeping the intestinal barrier intact and healthy (Mars et al., 2020). A subset of IBS patients have an altered hypoxanthine metabolism that involves both the host and the gut, that sheding light on the importance of the microbiome and how this metabolite can affect symptoms (Mars et al., 2020).

Bacterial Compounds and IBS-D
Another bacterial compound that may be important in IBS is tryptamine (Mars et al., 2020). IBS-D patients have been observed to have increased bacteria production of tryptamine. Tryptamine increases water secretion in the intestines. The resultant reduction in bacteria metabolism of bile acids would lead to high levels of primary bile acids, which can, in turn, irritate the colon and increase water secretion leading to diarrhea.

Constipation-Predominant IBS
In some IBS-C patients, decreased production of short-chain fatty acids (such as hypoxanthine) is observed. It has been hypothesized by Mars et al. (2020) that alterations in purine metabolism and related substances could contribute to the development their IBS symptoms. Further research is, however, needed to better understand the specific mechanisms and interactions between hypoxanthine and IBS (Mars et al., 2020). Because short-chain fatty acids increase movement of stool in the intestine, perhaps native or engineered bacteria that produce short-chain fatty acids or tryptamine can be used to treat the symptoms of IBS-C patients.

Intestinal Barrier and Resistant Starches
The intestinal barrier lets nutrients in and helps keep harmful bacteria out of the intestine (Birt et al., 2013). Resistant starchyes also play an important roll in keeping the intestinal barrier intact. Resistant starchyes cannot be digested in the small intestine and pass to the colon to be fermented by microbiota (Birt et al., 2013). When a resistant starch is fermented in the intestines, the by-products are short-chain fatty acids, the most common of which is butyrate. Butyrate is the main food for cells in the colon. If the colon cells lack butyrate, cell leakage can occur. Butyrate also assists with pathways that regulate the genes that affect immunity, inflammation, energy, and appetite, which are believed to provide anti-inflammatory and anticarcinogenic protection (Fu, Liu, Zhu, Mou, & Kong, 2019). Resistant starchyes can be found in whole grains, greens, green bananas, and cooked and cooled starches such as a baked potato. Adding resistant starchyes to the diets of IBS patients may therefore provide an effective treatment strategy for controlling their IBS symptoms because a targeted food intervention of this nature may modulate the microbiome for improved homeostasis.

Implications for Nursing Practice
Until more individualized therapies are developed, targeting IBS from a dietary standpoint is worthwhile (Vedantam, Graff, Khakoo, Khakoo, & Pearlman, 2023). This is especially true if the intervention involves the implementation of a more diverse diet that can influence the microbiome in a positive way for IBS patients. Because many IBS patients report diet as a trigger, it is sensible in most cases to recommend a low FODMAP diet because the poorly absorbed makeup of these types of food leads to bloating and pain (Shaikh et al., 2023).

Although more research is needed on the specific pathways of IBS subtypes, keeping the microbiome ecosystem healthy is a worthwhile aim for all health providers when treating IBS patients. The importance of a healthy microbiome, and ways to promote it through dietary changes, is, something that all health-care providers can readily discuss with their patients. To promote the growth of beneficial gut bacteria, it is recommended that nursing and other providers include counseling on a diverse diet that includes soluble fiber, different types (colors) of vegetables, fruits, and resistant starchyes in their treatment plan for IBS patients. IBS patients should also be encouraged to avoid processed foods and artificial sweeteners that can exacerbate symptoms and inflammation.

Although more research is needed to understand fully the diet and microbiome relationship, it is not the only barrier that impacts nurses’ ability to deliver this much needed education for their IBS patients. Additional key barriers include time, reimbursement, space, and the motivation of the learner (Bastable, 2017). In some healthcare environments, administrators do not
prioritize patient education. Continued collaboration with nursing, providers, dietitians, and other members of the healthcare team is essential to assist IBS patients in improving their quality of life.

Conclusion

IBS is considered a high disease burden because it is associated with high healthcare costs and low work productivity. Additionally, IBS is linked to anxiety and depression, as well as an overall reduction in patient quality of life (Skaikh et al., 2023). The microbiome is made up of trillions of microorganisms that play a major role in digestion, absorption of nutrients, and the immune system. Although more research is needed on the exact mechanisms involved, disruptions to the microbiome, including a gut imbalance, appear to contribute to IBS. Overall, the gut microbiome plays a critical role in maintaining health, including the GI system, and there is great potential for more personalized interventions. When this ecosystem is disrupted, it can lead to illness.

A better understanding of alterations in the specific composition and function of the gut microbiome and changes in bacterial species and microbial metabolites can lead to individualized treatments of IBS. The latest research highlights that interventions focused on restoring and maintaining a healthy microbiome, through the use of probiotic and prebiotic supplements, following a low FODMAP and diverse diet, and FMT can provide effective ways to minimize IBS symptoms (Bull & Plummer, 2015). Although all of these treatment options have been shown to help, maximizing the benefits of these treatments requires new research to help hone in on the specific bacterial strains and biomarkers involved.

The microbiome affects homeostasis, immune responses, fermentation patterns, and neurotransmitter signaling. Although it is also known to play a role in IBS symptoms, further research is required to unravel the entangled mechanisms underlying this relationship so that more targeted management of IBS through microbiome-based interventions can be achieved. Although the microbiome only appears to play a role in IBS symptoms for a subset of patients, it is still nevertheless useful to incorporate dietary changes into the treatment plans of all IBS patients to assist with managing their symptoms.

Time is needed to help a patient make these dietary changes. First, the individual needs to be referred to a dietitian who has familiarity with the microbiome or the person must be encouraged to read a handout to start the conversation until more time can be found to support patient education. Diverse diets that help a patient to avoid trigger foods and encourage consuming resistant starches are a sensible starting point.

Although knowledge about the relationship between the microbiome and IBS continues to evolve, existing research demonstrates that the gut plays a critical role in the development of IBS and its symptoms. As research continues to explore this relationship, new paths for personalized treatment will continue to emerge.

REFERENCES


Sloane P. & T, 6(11), 99. doi:10.3390/jcm6110099


Copyright © 2024 Society of Gastroenterology Nurses and Associates.